

I. INTRODUCTION

This paper is submitted in response to the Office Action mailed April 26, 1995, for which the three-month date for response was July 26, 1995.

A request for a three-month extension of time to respond is included herewith along with the required fee. This three-month extension will bring the due date to October 26, 1995, which is within the six-month statutory period. Should such request or fee be deficient or absent, consider this paragraph such a request and authorization to withdraw the appropriate fee under 37 C.F.R. §§ 1.16 to 1.21 from Arnold, White & Durkee Deposit Account No. 01-2508/UTSK:142/BAH.

In addition, the appropriate fee for the additional seven claims is enclosed.

Reconsideration of the application is respectfully requested.

II. AMENDMENTS

Please make the following amendments:

A. Amendments To the Specification

Page 9, line 25, after "wavelengths," insert ☒ -six wavelengths
in an absorbance subset--;
line 32, after "wavelength", insert ☒ -forms a
scattering subset and--.

On page 10, line 24, add the following new paragraphs:

B3 -- In particular, the present invention contemplates a method of determining the concentrations of a plurality of constituent components of unaltered whole blood of unknown composition. First, a plurality of substantially monochromatic radiation wavelengths is generated, each wavelength of an absorbance subset of the plurality of wavelengths having been selected by its ability to distinguish the constituent components and having been selected to minimize the effects of radiation scattering and to maximize radiation absorbance by said constituent components, and each wavelength of a scattering subset of the plurality of wavelengths having been selected to maximize the effects of radiation scattering by unaltered whole blood relative to the effects of radiation absorbance by unaltered whole blood. Then, a sample of unaltered whole blood of unknown composition is irradiated with the plurality of radiation wavelengths, through a depth of the sample chosen to minimize radiation scattering by unaltered whole blood. Next, intensities of the radiation wavelengths, after passing through the depth of the sample are detected at a distance from the sample, and over a detecting area, both chosen to minimize the effects of radiation scattering by unaltered whole blood on the determination of concentrations of the constituent components. Finally, the concentrations of the plurality of constituent components of the sample of unaltered whole blood corrected for the effects of radiation scattering are calculated, based upon detected intensities of each of the plurality of radiation wavelengths, and based upon predetermined molar extinction coefficients for each of

the constituent components at each of the plurality of radiation wavelengths.

cont 103
The depth of the sample may be in the range of 80 to 150 micrometers, preferably approximately 90 micrometers. The detecting area may be at least approximately 150 square millimeters, preferably approximately 600 square millimeters. The distance from the sample may be within the range of 0 to 10 millimeters, preferably approximately 1 millimeter. The detecting step may be performed over a cone of radiation emanating from the sample with a half-angle of at least approximately 30 degrees, and preferably at least approximately 70 degrees.

Another feature of the invention is the correction of the calculated concentrations of the constituent components for the effects of finite spectral bandwidth of the substantially monochromatic wavelengths on the extinction coefficients of each constituent component.

In accordance with one embodiment of the invention, the plurality of constituent components include HbO_2 , HbCO , Hi and Hb , the method further comprising, before the generating step, selecting four radiation wavelengths by computing an error index for each of HbO_2 , HbCO and Hi as the sum of the absolute values of the errors that are induced in the measurement of relative concentrations of HbO_2 , HbCO and Hi due to a change in optical

density measurements; and selecting a quadruple of radiation wavelengths having minimum error indices. Each wavelength in the quadruple of radiation wavelengths may be within the range of 510 to 630 nanometers. Exemplary quadruples include: 522, 562, 584 and 600 nanometers; 518, 562, 580 and 590 nanometers; and 520.1, 562.4, 585.2 and 597.5 nanometers.

cont
B3
In accordance with another embodiment of the invention, the constituent components may include bilirubin. Then, the method further comprises, before the generating step, selecting a radiation wavelength within the range of 475 to 500 nanometers as the radiation wavelength for the measurement of bilirubin, and preferably 488.4 nanometers.

In accordance with yet another embodiment of the invention, the constituent components may include sulfhemoglobin. Then, the method further comprises, before the generating step, selecting a radiation wavelength within the range of 615 to 625 nanometers as the radiation wavelength for the measurement of sulfhemoglobin, and preferably 621.7 nanometers.

The method of the present invention may further include correcting the calculated concentrations of constituent components for the effects of light scattering by red blood cells. This correction may include correcting the calculated concentrations of constituent components as a function of the relative concentrations

of the constituent components, and may include iteratively determining a red blood cell scattering vector for the particular composition of the whole blood sample being analyzed; and using the red blood cell scattering vector to correct the calculated constituent component concentrations.

cont
B3
The method of the present invention may further include correcting the calculated constituent component concentrations for the effects of non-specific light scattering. This correction may be accomplished by iteratively determining a non-specific scattering vector for the particular composition of the whole blood sample being analyzed; and using said non-specific scattering vector to correct the calculated constituent component concentrations.

The method also contemplates simultaneously correcting the calculated concentrations of constituent components for the effects of light scattering by red blood cells and for the effects of non-specific light scattering.

Yet another feature of the present invention is the correction of the calculated concentrations of constituent components as a function of wavelength.--

Page 16, line 15, change "measuring" (second occurrence) to --
an absorbance subset of--